

Program Announcements (PA'S)

Association of Arthritis & Musculoskeletal Diseases With HIV Positivity & AIDS

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

The Arthritis and Muscle Biology Programs of the National Institute of Arthritis and Musculoskeletal and Skin Diseases invite research grant applications to study arthritis and inflammatory muscle and other rheumatic conditions associated with HIV infection and/or AIDS. This program announcement is to encourage research grant applications for basic, clinical, and epidemiologic research. Research mechanisms to support these investigations include traditional research grants (RO1), Clinical Investigator Awards (K08), and First Independent Research Support and Transition (FIRST) Awards (R29).

Several investigators have reported the co-occurrence of HIV antibody positivity or frank AIDS with Reiter's Syndrome and other rheumatic disorders. It is unknown whether a causal biological connection exists between certain arthritides and HIV infection or some of these co-occurrences are merely coincidental.

Certain arthritides and inflammatory muscle diseases and other rheumatic disorders may be found more frequently in HIV-positive individuals and AIDS patients than in the general population, according to reported observations. The frequency, spectrum, and natural history of these conditions in HIV-positive individuals, including AIDS cases, are unknown. It has also been noted that a spectrum of disease encompassing Reiter's syndrome and psoriasis, in particular, appears to be more severe and increasingly difficult to control as signs of immunodeficiency develop. Myositis may be an early presenting feature of HIV infection, and myopathy secondary to zidovudine therapy has been reported.

Safety and efficacy of drugs used in the management of arthritis, inflammatory muscle diseases, and other rheumatic disorders have not been formally assessed in HIV-positive individuals. Recent case reports have suggested that immunosuppressive drugs, particularly methotrexate, used widely at present in the management of rheumatoid arthritis and psoriatic arthritis, may accelerate AIDS in HIV-infected individuals.

A previous program announcement (see NIH Guide for Grants and Contracts,

Vol. 17, No. 12, April 1, 1988) was published to encourage research in this area. The current solicitation is intended to further stimulate basic, clinical, and epidemiologic research related to arthritis, inflammatory muscle diseases, and other rheumatic manifestations in HIV-positive individuals, including those who have AIDS. In addition, it is expected that the increased frequency of these diseases in HIV-positive individuals will provide unusual opportunities for research on the pathogenesis and accelerating factors in Reiter's syndrome, myositis, and other rheumatic diseases of uncertain etiology.

Among the broad spectrum of basic research projects encouraged are studies of disease pathophysiology and genetics. Clinical studies may include prevention of morbidity and mortality or amelioration of arthritis, inflammatory muscle disease, and other rheumatic complications. Epidemiologic studies may focus on etiology, risk factors for disease development and severity, natural history of disease, and prognosis for developing disease. This includes AIDS and arthritis, inflammatory myopathy, and other rheumatic syndromes as well as descriptive studies of incidence, prevalence, morbidity, and mortality.

Investigators are encouraged to work with existing, or proposed, longitudinal data collection resources and cohorts of patients. Populations that may be included are those at increased risk for HIV infection, as well as HIV-positive cohorts who are clearly defined by their source of exposure. Investigators are encouraged to use existing cohorts, such as the Multicenter AIDS Cohort Study (MACS), the HIV Pulmonary Complications Study, and the AIDS Clinical Trials Group patients.

SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants/offerors are urged to

assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority populations groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' population, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

ELIGIBILITY

Nonprofit organizations and institutions, governments and their agencies, for-profit organizations, and individuals are eligible to apply. Foreign institutions are eligible to apply.

APPLICATION PROCEDURES

Applications will be accepted in accordance with the announced receipt dates for unsolicited AIDS R01 and R29 applications, January 2, May 1, and September 1 of each year. AIDS investigator-initiated applications received on these dates by the Division of Research Grants will undergo expedited review. Applicants for the K08 award must submit applications to meet the receipt dates listed in the instructions for that mechanism.

All applications must be submitted on form PHS 398 (rev. 10/88). Application kits are available in the business or grants and contract office at most research and academic institutions. Additional application kits may be obtained from the office of Grants Inquiries, Division of Research Grants (DRG), NIH, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. The phrase, "Association of Arthritis, Inflammatory Muscle Diseases and Other Rheumatic Manifestations with HIV Positivity and AIDS, PA-91-82" must be typed at item 2 of the face page of the application form 398 (rev. 10/88). The original and 24 copies for receipt dates of an R01 or R29 application submitted for expedited review must be sent to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

REVIEW PROCEDURES AND CRITERIA

Applications in response to this solicitation will be reviewed in competition with other research grant applications and in accord with the expedited NIH peer review procedures for AIDS-related research. To expedite the review, investigators must submit PHS human subject certifications and animal verifications with the applications. Applications will be reviewed first for technical merit by initial review groups and then by an appropriate national advisory council. The review criteria customarily employed by the NIH for research grant applications will prevail.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from the Program Director of the GCRC must be included with the application material.

All PHS and NIH grant policies governing research project grants apply to applications received in response to this program announcement. Applications will be referred in accordance with customary procedures of the DRG.

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This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.